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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Igor Stagljär

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EXAMINER

JOIKE, MICHELE K

ART UNIT

PAPER NUMBER

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/509,507	Applicant(s) STAGLJAR ET AL.	
	Examiner MICHELE K. JOIKE	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 48-81 is/are pending in the application.
- 4a) Of the above claim(s) 69 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 48-68, 70-73 and 75-81 is/are rejected.
- 7) ☒ Claim(s) 74 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 48-81 are pending in the instant application. Claim 69 is withdrawn; claims 48-68 and 70-81 are examined. Any rejection of record in the previous Office Action, mailed October 3, 2008 that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Objections

Claim 57 is objected to because of the following informalities: “plamid” should be “plasmid” in lines 7 and 13. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48-55, 57-62, 64-67 stand rejected under 35 U.S.C. 102(b) as being anticipated by Stagljär et al (PNAS 95: 5187-5192, 1998, specifically pp. 5187, 5191 and figure 2). This rejection is maintained for reasons of record in the previous office action mailed October 30, 2007.

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Response to Arguments Concerning Claim Rejections – 35 USC § 102(b) and 103(a)

Applicant's arguments filed July 8, 2009 have been fully considered but they are not persuasive.

The following grounds of traversal are presented:

Applicants argue that the bait and prey vectors that are maintained episomally. In contrast, Stagljär's bait vector is integrated into the yeast genome. The term "maintained episomally" is consistently used as the opposite of "integrated" in patents covering analogous art including the Examiner's own art unit. Additionally, the claims have been amended to indicate that the vectors are plasmid constructs. Plasmids replicate autonomously. This clarifies that the bait and prey vectors are integrated. Dependent claims further define the plasmids as having a CEN/ARS or 2 micron origin of replication for propagation.

There is no promoter in pRS305 as part of the expression cassette as set forth in claim 66.

Ehrhard et al do not cure the deficiencies of Stagljär.

The office stated that the motivation to combine Ecker with Stagljär is that the CUP1 promoter can be partially repressed, which leads to lower levels of expression. There is no rationale as to why one skilled in the art would desire this.

The office stated that the Clarke teaches the CEN/ARS vector as a low copy vector. There is no rationale as to why one skilled in the art would desire this. Furthermore, CEN/ARS plasmids are less stable than normal yeast chromosomes.

These arguments are not found persuasive for the following reasons.

Both types of vectors are maintained episomally. Applicants do not define "episomally" in the specification. Absent a definition by the Applicant, the Examiner is giving the word its broadest reasonable interpretation. Merriam-Webster's dictionary defines "episomal" as "a genetic determinant (as the DNA of some bacteriophages) that can replicate autonomously in bacterial cytoplasm or as an integral part of the chromosomes." Therefore, even integrated vectors are maintained episomally. Episomal maintenance was not an issue in US 7,435,546, and the Examiner cannot comment on patents issued by other Examiners. Plasmids can be integrated into the genome, however, Stagljar teaches plasmids with either a CEN/ARS or 2 micron origin of replication. See, for example, figure 3. Therefore, they also have the ability to replicate autonomously.

While there may be no promoter as part of the expression cassette described in claim 66 in pRS305, pRS305 becomes integrated next to the Wbp1 promoter as noted by Applicant. Since the Examiner is interpreting episomal maintenance to include integration, the vector has a promoter.

As discussed above, there are no deficiencies for Ehrhard to cure.

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The Examiner also stated the CUP1 promoter can be induced to achieve high level of expression as well, the rational being that one of skill in the art would find benefit in a promoter can be regulated for either low or high levels of expression.

Stagljar teaches plasmids with a CEN/ARS. Just because they did not use it in all of their plasmids, does not mean it is not an obvious choice. Low expression of genes can be desirable in many situations, for example to aid in stability. Plasmids are generally less stable than chromosomes, and one of skill in the art would know that. However, Clarke also teaches that CEN/ARS plasmids greatly increase mitotic stability.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 68 and 70 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljär et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Ehrhard et al.

Claims 63 and 75 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljär et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Ecker et al.

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Claims 71-73 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljär et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Clarke et al.

Claim 56 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljär et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Wedegaertner et al and Friedberg et al.

Stagljär et al teaches all of the limitations as described previously. However, they do not teach the protein attached artificially to the membrane and the signal sequence encoding a membrane anchor.

Wedegaertner et al (J. Biochem. 270(2): 503-506, 1995, especially p. 503) teach lipid modifications of G proteins so they will attach to the membrane. (Applicants discuss in their specification that fatty acid modification is a means for artificially attaching proteins.)

Friedberg et al (Biochem J. 303: 967-972, 1994) teach an anchor signal sequence attached to a protein.

The ordinary skilled artisan, desiring to artificially attach a protein to the membrane via a membrane anchor, would have been motivated to combine the teachings of Stagljär et al teaching a split-ubiquitin system for detecting the interaction between two membrane bound proteins, as described above, with the teachings of Wedegaertner et al, teaching modifying proteins so they will attach to the membrane with the teachings of Friedberg et al teaching an anchor signal sequence because

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Friedberg et al teach the attaching a membrane anchor signal sequence to a protein will anchor the protein to the membrane and that heterologous membrane anchors can be used to transport proteins. It would have been obvious to one of ordinary skill in the art to attach a protein to the membrane because Wedegaertner et al teach that different lipid modifications affect specific protein-protein interactions and localization to specific sites. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 63, 75 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Mumberg et al.

Applicants claims use of a promoter that confers low level expression, wherein the promoter is CYC1.

Stagljar et al teaches all of the limitations as described above. They teach use of the CUP1 promoter in the pRS314(Nubi-ALG5) vector, however, they do not teach the CYC1 promoter.

Mumberg et al (Gene 156: 119-122, 1995) teach use of the CYC1 promoter for expression in yeast.

The ordinary skilled artisan, desiring to use a CYC1 promoter, would have been motivated to combine the teachings of Stagljar et al teaching a split-ubiquitin system for

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detecting the interaction between two membrane bound proteins, as described above, with the teachings of Mumberg et al, teaching use of the CYC1 promoter for expression in yeast because Mumberg et al teach that the CYC1 promoter can be altered to make a weak promoter for a lower level of expression, which can be desirable if low levels of a gene need to be expressed, for example, a toxic gene. It would have been obvious to one of ordinary skill in the art to use CYC1 because Mumberg et al teach that CYC1 is a constitutive promoter, which is desirable if one skilled in the art does not want to induce expression. In other words, the promoter can be regulated for low or high levels of expression. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 63, 75 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Ecker et al.

Applicants claims use of a promoter that confers low level expression, wherein the promoter is CUP1.

Stagljar et al teaches all of the limitations as described above. They teach use of the CUP1 promoter in the pRS314(Nub1-ALG5) vector, however, they do not teach the CUP1 promoter in the bait vector.

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Ecker et al (J. Biochem. 262(8): 3524-2527, 1987, especially p. 3524-2525)

teach use of the CUP1 promoter for expression of the ubiquitin gene in yeast.

The ordinary skilled artisan, desiring to use a CUP1 promoter, would have been motivated to combine the teachings of Stagljar et al teaching a split-ubiquitin system for detecting the interaction between two membrane bound proteins, as described above, with the teachings of Ecker et al, teaching use of the CUP1 promoter for expression of the ubiquitin gene in yeast because Ecker et al teach that the CUP1 promoter can be partially repressed, which would lead to lower levels of expression. It would have been obvious to one of ordinary skill in the art to use CUP1 because Ecker et al teach that the important point is that the CUP1 promoter can be induced by copper, and if desired, high levels of expression can be attained. In other words, the promoter can be regulated for low or high levels of expression. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 71-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stagljar et al as applied to claims 48-55, 57-62, 64-67 above, and further in view of Clarke et al. New claims 78-81 are added to the rejection.

Applicants claims use of low copy vector, wherein the vector has a CEN/ARS origin of replication.

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Stagljar et al teaches all of the limitations as described above. They teach use of the CEN/ARS origin of replication in the Nubl-ALG5 vector, however, they do not teach the CEN/ARS origin of replication in the bait vector.

Clarke et al (Ann. Rev. Genet. 19:29-56, 1985, especially pp. 32-33) teach use of the CEN/ARS vector as a low copy vector.

The ordinary skilled artisan, desiring to use a CEN/ARS vector, would have been motivated to combine the teachings of Stagljär et al teaching a split-ubiquitin system for detecting the interaction between two membrane bound proteins, as described above, with the teachings of Clarke et al, teaching use of the CEN/ARS vector because Clarke et al teach that the copy number of a CEN/ARS vector is only 1-2 copies per cell. It would have been obvious to one of ordinary skill in the art to use a CEN/ARS vector because Clarke et al teach that the CEN/ARS vector greatly increases mitotic stability. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Allowable Subject Matter

Claim 74 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K. Joike/
Examiner, Art Unit 1636

Michele K. Joike
Examiner
Art Unit 1636